CLINICAL GUIDELINE

Vitamin D: Prevention & Treatment of Deficiency in Adults
SCOPE:
This guidance gives advice on how to treat adults who are at risk of or who are known to have deficient /insufficient levels of vitamin D.
This guidance is written for primary and secondary care prescribers. It refers to adults only.

BACKGROUND:
In February 2012; the UK Departments of Health issued advice on use of vitamin D supplements to at risk groups. This advice can be found here. NICE published further guidance in November 2014 which aimed to increase supplement use to prevent vitamin D deficiency among at-risk groups, identified in the Department of Health advice. NICE guidance can be found here.

In brief the Departments of Health recommend for adults that:
- All pregnant and breastfeeding women should take a daily supplement containing 10 micrograms (400 units) of vitamin D, to ensure the mother’s requirements for vitamin D are met and to build adequate fetal stores for early infancy
- People aged 65 years and over and people who are not exposed to much sun should also take a daily supplement containing 10 micrograms (400 units) of vitamin D

Most of the population of the West of Scotland has low levels of vitamin D because of low levels of UV/sun exposure. The important clinical syndrome that can result from deficiency of vitamin D is osteomalacia – a syndrome characterised by malaise, multifocal bone pain with tenderness and proximal myopathy. Osteomalacia is associated with abnormal biochemistry – high serum alkaline phosphatase, serum calcium low/low normal, serum PTH high & low vitamin D, usually <30nmol/L. The prime aim in giving vitamin D to our patients is to prevent this vitamin D deficiency syndrome. Diverse health problems ranging from MS to heart disease, from TB to cancers at various sites have been ASSOCIATED with low levels of vitamin D (and with higher latitude) BUT there is NO or INSUFFICIENT evidence to support a causal link between low vitamin D and any of these problems; furthermore there is no evidence that giving vitamin D alters the incidence of any of these conditions.

Vitamin D levels of <30nmol/L are generally considered to be ‘deficient’ (however even at this level most patients do not have osteomalacia). Vitamin D levels of above 50nmol/L are generally viewed as ‘sufficient’. In terms of description; vitamin D levels in the range of 30-50nmol/l are described as insufficient however use of vitamin D supplements are often not required in this context - see National Osteoporosis Society (NOS) - Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management (https://nos.org.uk/media/2075/vitamin-d-and-bone-health-quick-guide-adults.pdf).
The vitamin D that is routinely measured in the laboratory is 25-hydroxyvitamin D₃ (25(OH)D₃). This compound is inactive, but is stable, and serum levels correlate reasonably well with vitamin D activity. This is the vitamin that is measured when "vitamin D" measurement is requested through biochemistry.

1,25-di-hydroxyvitamin D (1,25(OH)₂D₃) is the biologically active form of vitamin D. This can be measured biochemically but it is unstable and levels do not correlate well with vitamin D activity. Measurement of 1,25(OH)₂D₃ should be reserved for patients with hypercalcaemia complicating granulomatous disease such as sarcoidosis or in patients with vitamin D resistant rickets. There may rarely be course to measure1,25(OH)₂D₃ in patients taking calcitriol or alfacalcidol.

WHEN TO MEASURE VITAMIN D:
1. Patients with low adjusted serum calcium (<2.2mmol/L) and/or where other blood results suggest possible osteomalacia
2. Patients with malabsorption syndromes
3. CKD (eGFR <30) - measurement in this context should usually be carried out by specialist clinics only.

WHEN NOT TO MEASURE VITAMIN D:
1. Patients prescribed Vitamin D at daily doses of less than 5000 units/day. Toxicity is unlikely at these doses and where required should be undertaken by secondary care specialists.
2. Patients on alfacalcidol or calcitriol (not measured by assay – see 1,25(OH)₂D₃ above)
3. Vitamin D is not a test that is helpful in investigation of tiredness, chronic fatigue / fibromyalgia or non-specific aches and pains (with normal bone biochemistry).

HOW FREQUENTLY TO MEASURE VITAMIN D:
Follow-up measurements are generally not required but there are occasional exceptions, for example in patients with malabsorption with suboptimal Vitamin D. But repeat testing is only appropriate after at least 6 months’ supplementation and is available at specialists’ request. Current evidence based practice shows that measurement of vitamin D should not be required more than once a year in routine clinical practice and as such vitamin D analysis will not be performed more frequently, unless specifically arranged and agreed with a biochemist.

PRESCRIBING VITAMIN D:
See the following flowcharts for advice on when supplementation of vitamin D is indicated and what to prescribe;
- Flowchart 1 - Vitamin D: Prevention & Treatment of Deficiency in Adults
- Flowchart 2 - Vitamin D: Deficiency in Adults in the context of (or at increased risk of) osteomalacia, osteoporosis or increased risk of fracture

Guideline authors: Thanks to NHS Greater Glasgow and Clyde for sharing their guidance. Amended by NHSL Clinical Laboratory Services and NHSL Osteoporosis Service.

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Flowchart 1 – Vitamin D: Prevention & Treatment of Deficiency in Adults

Which patient population are you managing?

- Patients with;
  - Proven or possible osteomalacia
  - Osteoporosis
  - Increased risk of fracture

Refer to Flowchart 2 below

- Pregnant or breastfeeding women particularly teenagers and young women. Vitamin D blood measurement NOT required.

Department of Health\(^1\) recommends a daily supplement containing 10 micrograms (400 units) of vitamin D. High strength formulations are not recommended in pregnancy or breastfeeding.

Healthy start vitamins are available from community pharmacy for eligible pregnant women and women with a child under one year old and contain the correct amount of vitamin D for this purpose. See https://www.healthystart.nhs.uk/for-health-professionals/healthy-start-resources/ for further details

- People aged 65 years and over who are not exposed to much sun. Vitamin D blood measurement NOT required.

Department of Health\(^1\) recommends a daily supplement containing 10 micrograms (400 units) of vitamin D.

Supplements are available to buy over the counter.

- Other high-risk asymptomatic patient groups. Vitamin D blood measurement NOT required:
  - Patients with dark skin
  - Institutionalised/housebound patients
  - Chronic alcohol misusers
  - Vegetarians/vegans
  - Obese patients
  - People who cover up (e.g. Muslim men and women)
  - Medical risk factors: renal, hepatic disease unless attending specialist clinics,
  - Specific medicines (e.g. anticonvulsants and anti-retrovirals)

Give advice on regular sun exposure (Panel 2), dietary sources of vitamin D (Panel 1) and buying the counter vitamin D supplements particularly in the winter.

Panel 1: Dietary Sources of Vitamin D\(^2\)
- Oily fish
- Cod liver oil or other fish oils
- Eggs
- Fortified breakfast cereals (see individual product packaging)
- Margarine
- Infant milk formula

Panel 2: Sun exposure advice\(^3\)
When possible, only a limited amount of time should be spent in strong sunlight. People who choose to expose their skin to strong sunlight to increase their vitamin D status should be aware that prolonged exposure (for example, leading to burning or tanning) is unlikely to provide additional benefit. Exposing commonly uncovered areas of skin such as forearms and hands, for short periods when in strong sunlight provides vitamin D. (Longer periods of exposure may be needed for those with darker skin.)

3. NICE 34 Sunlight exposure: risks and benefits available at https://www.nice.org.uk
Flowchart 2 - Vitamin D: Deficiency in Adults in the context of (or at increased risk of) osteomalacia, osteoporosis or increased risk of fracture

**Osteomalacia present?** (comprising non-arthritis bone pain; low vitamin D and raised PTH; raised ALP and calcium low/normal)

**YES**

Are vitamin D levels known?
See box A for when to measure vitamin D levels

**NO**

**Vitamin D <30 nmol/L**
Prescribe a loading dose regime of 300,000 units over 6 to 8 weeks. See NHSL Formulary for current options and dose regimes. Thereafter maintenance dose as per specialist advice.

**Vitamin D 30-50 nmol/L**

Prescribe a loading dose of 300,000 units over 6 to 8 weeks. See NHSL Formulary for current options and dose regimes. Thereafter maintenance dose 800 units once daily.

30–50 nmol/L may be inadequate in some people – See NOS guidance for further information. See point 1 in Box B: special considerations

**NO**

Assess whether to measure vitamin D

**Vit D Measuring required**

Is patient on treatment with bisphosphonate/denosumab or on bisphosphonate drug holiday?

**YES**

Does the patient have documented hypercalcaemia

**NO**

Refer to Flowchart 1 Vitamin D: Prevention & Treatment of Deficiency in Adults (above)

**Box A: Measuring vitamin D levels**

1. Patients with low adjusted serum calcium (<2.2 mmol/L) and/or possible osteomalacia
2. Patients with malabsorption syndromes
3. CKD (eGFR <30), measurements will be carried out by specialist clinics only

**Box B: Special considerations**

1. If fracture / osteoporosis and for IV zoledronic acid or SC denosumab, give 100,000 units colecalciferol orally once only and then treat with appropriate ongoing calcium and vitamin D (NHSL Formulary) or if calcium contraindicated with separate colecalciferol supplement.
2. Patients with malabsorption such as coeliac disease / pancreatic insufficiency (e.g. cystic fibrosis) or with chronic liver disease, & low Vitamin D should be treated as for patient with a vitamin D level of <30 nmol/L unless osteomalacia in which case follow guidance above.
3. Patients with chronic kidney disease (& eGFR <30) merit discussion with specialists.

Notes - The use of vitamin D in patients with Primary Hyperparathyroidism should be determined through specialist referral to Endocrinology. Potent vitamin D analogues such as calcitriol or alfalcacidol are typically reserved for patients with renal osteodystrophy or for patients with Primary Hypoparathyroidism and should be used in the context of guidance from appropriate specialists - as they carry risk of hypercalcaemia / hypercalcina.